

Amendments To the Specification

On page 16, please replace the paragraph below the table with the following amended paragraph:

Note that the sequence identity is defined as the percentage of nucleotides between two DNA sequences that are identical in the same location along the two genes. ~~comparisons~~ Comparisons of these predictions against experimental data reveal good agreement, particularly in light of the fact that there are no adjustable parameters in the modeling framework of the present invention. The only parameters are the free energy contributions used unchanged from literature sources (SantaLucia, J., Jr. (1998) *Proc. Natl. Acad. Sci. USA* **95**, 1460-1465). Therefore, no reparameterization is needed when either the experimental conditions or the sequences to be shuffled change, thus providing a versatile framework for comparing different protocol choices and setups.

On page 17, please replace the paragraph starting at line 5 with the following amended paragraph:

Results from the first example evidence that the effect of annealing temperature is captured effectively using the modeling framework of the present invention. ~~only~~Only after the unusually low annealing temperature of 25 degrees Celsius employed in the experiment was entered in the simulation model did predictions align with the experimentally observed crossover averages. The second example led to the identification of silent crossovers. Originally, the simulation model severely overestimated the total number of crossovers. Closer inspection revealed that this was due to the formation of heteroduplexes, between fragments and the growing template, sharing perfect sequence identity along the overlapping region. Upon extension these heteroduplexes gave rise to completely undetectable crossovers (i.e. silent)

whose signature was detected computationally. After the reassembly algorithm was revised to exclude silent crossovers, the simulation model predictions agreed with the results of the experiments.